UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/531,855	11/02/2005	Patrick Van Berkel	089995-000000US	4048

20350 7590 02/07/2008
TOWNSEND AND TOWNSEND AND CREW, LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

EXAMINER	
HIRIYANNA, KELAGINAMANE T	
ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
02/07/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/531,855	BERKEL ET AL.	
	Examiner	Art Unit	
	Kelaginamane T. Hiriyanna	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11,13 and 16-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11, 13 and 16-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on 11/19/2007 in response to office action mailed on 06/01/2007has been acknowledged.

Claims 1-11, 13; 16, 18 and 21 are amended.

Claims 12, 14-15 are cancelled.

Claims 1-11, 13 and 16-22 *are pending and are examined in this office action. Applicants are required to follow Amendment Practice under revised 37 CFR §1.121. The fax phone numbers for the organization where this application or proceeding is assigned is* ***571-273-8300.***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The references cited herein are of record in a prior Office action.

Claim Objections

Claims 2-11 are objected to because of the following formalities: While claiming dependence on the subject of previous claim referring to "The" subject of previous claim rather than "A", is proper format. Accordingly, "A recombinant" in claims 2-11 should read "The recombinant". Appropriate correction is required.

Claim Rejections - 35 USC § 112

Claims *1-11 and 13* are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The scope of invention as claimed encompasses compositions or products of a recombinant C1 inhibitor of any type or a C1 inhibitor derived from any animal species and use of any modifying enzyme of O-linked carbohydrate.

At the best the specification teaches a recombinant human CI inhibitor (rhC1INH) and a pharmaceutical composition and use of compositions/products of the same. Further the specification only teaches O-linked carbohydrate modifying enzymes ST3Gal I and ST3Gal III.

The specification does not disclose compositions of any other C1 inhibitor other than rhC1INH. Further the specification does not teach any other O-linked carbohydrate modifying enzymes other than ST3Gal I and ST3Gal III. Thus the number of examples provided does not commensurate with the scope and breadth of instant claims.

Applicant is referred to the guidelines for ***Written Description Requirement*** published January 5, 2001 in the Federal Register, Vol.66, No.4, pp.1099-1110 (see <http://www.uspto.gov>). The disclosure of a single species is rarely, if ever, sufficient to describe a broad genus, particularly when the specification fails to describe the features of that genus, even in passing. (See In re Shokal 113USPQ283(CCPA1957); Purdue Pharma L. P. vs Faulding Inc. 56 USPQ2nd 1481 (CAFC 2000). In analyzing whether the written description requirement is met for the genus claim, it is first determined whether a representative number of species have been described by their complete structure. Next, it is determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics (i.e. conserved motifs or domains).

Since the specification fails to disclose other claimed compositions that contained sufficient number of examples of C1 inhibitors and/or O-linked carbohydrate modifying enzymes, it is not possible to envision the broadly claimed compositions of C1 inhibitors and O-linked carbohydrate modifying enzymes would have same structure and properties. One cannot describe what one has not conceived. (See Fiddes v. Baird, 30 USP2d 1481 at 1483). Therefore, the lack of disclosure in the specification is not deemed sufficient to reasonably convey to one skilled in the art that the applicants were in possessions of the huge genera recited in the claims at the time the application was filed. Furthermore the possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with *sufficient relevant identifying characteristics* (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had

possession of the claimed invention. *See, e.g., Pfaff v. WellsElectronics, Inc., 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406; Amgen, Inc. v. Chugai Pharmaceutical, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991).* In the instant case the compositions as claimed has been defined only by a statement of function that broadly encompasses any C1 inhibitor and/or any O-linked carbohydrate modifying enzyme which conveyed no distinguishing information about the identity of the broadly claimed species. Accordingly one of skill in the art would conclude that applicant was not in possession of the claimed genus because a description of a single member of this genus would not be representative of claimed genus of compounds and is insufficient to support the claim in its present scope.

Claims 1-11, 13 and 16-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a C1 inhibitor that is changed in its circulatory half-life by a O-linked carbohydrate modification in vitro and a method of in vitro modification of O-linked carbohydrate moieties on C1 inhibitor is not enabled for any method for changing the circulatory half-life of C1 inhibitor directly in vivo by a specific modification modification of its O-linked glycosylation, in any cell line in vivo or in any non-human transgenic animal as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims for the reason of record as set forth in the previous office action mailed on 06/01/2007.

In Response to Arguments of 11/19/2007:

Applicant amends claims to reflect in vivo modifications in cell lines and non human animals. Applicant argues therefore concerns over the enablement of the scope of the claim encompassing in vivo modulation of O-linked glycosylation in proteins is overcome because the amended claims restrict the scope of in vivo modulation to non-human transgenic animals only.

Applicants' arguments are however, found not persuasive because firstly the primary Claim 16 as amended still encompasses in its breadth in vivo modulation of O-

linked glycosylation of any proteins in any non-human animal by co-expressing the protein and the O-glycosylation modifiying enzymes.

The applicant however, does not describe even a single enabled example wherein an enzyme or a gene or a drug is used for modulating the O-glycosylation levels of any protein in any non-human animal. Further art at the time of invention does not describe any example where in vivo modulation of O-glycosylation of the C1-inhibitor has been induced. In the absence of an enabled example and/or a representative number of enabled examples in the specification regarding in vivo modulation of O-linked glycosylation of C1 inhibitor or other protein to commensurate with the breadth of the claims one of ordinary skill in the art would conclude that the invention as instantly claimed is unpredictable and 'undue'. Hence the rejection is maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-11 and 13 are rejected under 35 USC 102 (b) as being anticipated by Wolf et al., (2001, protein expression and purification 22:414-421; art of record).

The above claims are directed to a recombinant C1-inhibitor that is changed with regard to its plasma circulatory half-life by modification of an O-linked carbohydrate and a pharmaceutical composition comprising a recombinant C1 inhibitor.

Wolf teaches regarding production and purification of recombinant C1 inhibitor and the various glycosylations levels of C1INH (p.415, col.1, 2nd paragraph). Wolf further teaches the differences between native and recombinant molecules in terms of their

glycosylation and the importance of reduced O-glycosyaltion in hereditary diseases involving (p.419, col.2, 2nd paragraph). He further indicates engineered glycosylation pathways to obtain recombinant inhibitor (rC1INH) for clinical evaluation (p.420, col.1). The cited art thus anticipates the invention as claimed.

The cited art thus clearly anticipate the invention as claimed because the product namely " a recombinant C1 inhibitor" are physically the same as the prior art product and must have the same properties unless shown otherwise. "Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the prima facie case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. In re Best, 562 F.2d at 1255, 195 USPQ at 433. See also Titanium Metals Corp. v. Banner, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985)".

Claim Rejections - 35 USC § 103

Claims 16-22 stand rejected under 35 USC 103 (a) as being unpatentable over Paulson et al (1998, WO 98/31826), Shoenberger et al (1992, FEBS 314: 430-434), Wolf et al., (2001, protein expression and purification 22:414-421) and in view of Glaser et al (WO 92/03149) for the reason of record as set forth in the previous office action mailed on 06/01/2007.

In Response to Arguments of 08/17/2006:

Applicant argues that Paulsosn's reference is not relevant because he does not mention C1 inhibitors. Applicant further argues that 103 references provided

(Shoenberger, Wolf and Glaser) do not expressly teach the importance of O-linked glyosylations in changing circulatory half-life of the C1 inhibitor.

However, Applicants arguments are not found persuasive because firstly the Applicants instant method claims 16-21 are broad and encompass all glycoproteins and all glycoprotein-comprising compounds and hence the applied art is still relevant. The generic methods described in Paulsons for glycoproteins in general thus making it relevant with regard to claimed modulation of O-glycosylation of proteins in vitro in particular. Fourthly Paulson by describing a generic method regarding protein glycosylations and their role in circulatory half-life of glycoproteins anticipates all glyco proteins. Currently the rejection is restricted to broad claims encompassing all proteins in general. Thus the instant invention as claimed is obvious over the cited references. Hence the rejection is maintained.

Conclusion:

No claim allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner *Kelaginamane Hiriyanna Ph.D.*, whose telephone number is **(571) 272-3307**. The examiner can normally be reached Monday through Friday from 9 AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *Joseph Woitach Ph.D.*, may be reached at **(571) 272-0739.** The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). When calling please have your application serial number or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. For all other customer support, please call the USPTO call center (UCC) at (800) 786-9199.

Kelaginamane T. Hiriyanna
Patent Examiner
Art Unit 1633

AU1633